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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,259	11/06/2006	Edwin Pei Yong Chow	6565-76130-01	2433

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EXAMINER	
BECKHARDT, LYNDSEY MARIE	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
12/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,259	CHOW ET AL.	
	Examiner	Art Unit	
	LYNDSEY BECKHARDT	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *16-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 are currently pending. Claims 1-15 are currently under examination.

Priority

This application claims priority to PCT application PCT/SG04/00237, filed 08/04/2004. The effective filing date of the instant application is deemed to be 08/04/2004.

Information Disclosure Statement

Applicant argues that three references listed in the Information Disclosure Statement forms filed on September 11, 2008, December 16, 2008 and March 4, 2009 have not been considered, as Examiner has written no publication date next to the listed references. Applicant requests the Examiner considers these references.

In response, the references have now been considered and are cited on the enclosed Notice of References Cited.

Response to Arguments

Applicant's arguments, see page 5, filed 10/13/2009, with respect to objections have been fully considered and are persuasive. The objection of claims 6, 9 and 15 has been withdrawn.

Applicant's arguments with respect to prior art rejections have been considered but are moot in view of the new ground(s) of rejection. Applicant has amended claim 1, the sole independent examined claim, changing the scope. As such new rejections are applied below as a result of Applicant's amendment.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

New Rejections:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 10-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chieng et al (previously cited 07/14/2009, publication date: 1995) in view of Vandamme (Microemulsions as ocular drug delivery systems: recent developments and future challenges, publication date: 2002), Lui (previously cited 07/14/2009, publication date: 1997) and US 6,039,913 (patent date: 03/21/2000).

Chieng teaches microemulsions are thermodynamically stable, transparent, isotropic liquids consisting of water and oil phases stabilized by a surfactant or a combination of surfactant and co surfactant. The microstructure of a microemulsion depends on the composition of the system, one such structure being bicontinuous at intermediate water content. Bicontinuous structure of microemulsions has been extensively investigated. Recently an increase in interest has emerged in studying the formation of porous polymeric solids by polymerization of monomer-containing

microemulsions with bicontinuous structures (page 1941, first column, first paragraph). Materials used were methyl methacrylate (MMA), 2-hydroxyethyl methacrylate (HEMA) and ethylene glycol dimethacrylate (EGDMA). Dibenzyl ketone (DBK), sodium dodecylsulfate and dionized water were also used (page 1941, second column, first paragraph). A stock solution containing 20% SDS in water was prepared. The single-phase region of the microemulsion was determined visually by titrating a specific amount of MMA, HEMA and EGDMA with the stock solution (page 1941, second column, second paragraph). The composition contents in wt% are listed in Table 1 below.

Table 1 Microemulsion compositions used for polymerization[a]

Microemulsion system	Compositions (wt%)				Appearance of the system[b]	
	MMA	HEMA	SDS	Water	BP	AP
H4	57	38	1	4	C	C
H8	54	36	2	8	C	C
H12	51	34	3	12	C	C
H16	48	32	4	16	C	WY
H24	42	28	6	24	C	O
H32	36	24	8	32	C	O
H40	30	20	10	40	C	O
S14	36	24	14	26	C	O
MH55	30	30	8	32	C	O
MH37	18	42	8	32	C	WY
MH19	6	54	8	32	C	WY

[a]Weight ratio of MMA:HEMA was fixed at 3/2 for systems H4, H8, H12, H16, H24, H32, H40 and S14, while that for systems MH55, MH37 and MH19 varied from 5/5 to 3/7 and 1/9 respectively. EGDMA added was 4 wt% based on the total weight of MMA and HEMA, and photoinitiator DBK added was 0.3 wt% based on the total weight of each microemulsion sample

[b]BP = before polymerization; AP = after polymerization; C = clear; WY = white yellowish; O = opaque

(Table 1, page 1942)

The photoinitiator, DBK, was used for initiating the microemulsion polymerization (page 1942, first column, first paragraph).The phase behaviors of the microemulsion

was evaluated, and it was determined that a bicontinuous region was present in the microemulsion (page 1942, second column, first paragraph). A substantial increase in conductivity can be seen as the water content is increased from about 20% to 80%. This is attributed to the presence of biocontinuous structure in which both water an oil domains are interconnected with each other formed conducting channels (page 1943, first column, first paragraph). A continuous increase in viscosity is observed in the microemulsions on increasing the water content up to about 80%. This is because the number of droplets or channels increases on increasing water content which in turn increases the interactions between them (page 1943, first column, second paragraph). The microstructure became very distinctive for samples containing more than 20wt% water. For instance globular microstructure with the dimension of micrometers was seen. They stacked onto each other and the voids (pores) formed resembled the packing of a chromatographic column using fine particle materials. It is believed that these pores were interconnected and were water-filled spaces generated between the incompletely coalesced spherical aggregates (page 1943, column 2, second paragraph). Pores nearly round in shape of dimension ca 1-10um can clearly be seen in SEM micrograph. These pores might be derived from water domains of the polymerized microemulsion system (page 1945, first paragraph).

Chieng does not teach the inclusion of a drug dispersed in at least said second phase polymer matrix and releasable therefrom, wherein said drug is an ophthalmic drug. Chieng does not teach the use of C1-PEO-C11-MA-40 for a nonionic surfactant.

Liu teaches a transparent nanostructure polymeric materials have been produced from the direct polymerization of bicontinuous microemulsions using the macromonomer ω methoxy poly(ethylene oxide)$_{40}$ undecyl α methacrylate (C1-PEO-C11-MA-40) as a polymerizable nonionic surfactant. Besides the PEO macromonomer, the system also consisted of (MMA), (HEMA), EGDMA and water. The pore size of these transparent polymeric materials ranges from about 1 to 10 nm in diameter. The PEG filtration provide the direct evidence that bicontinuous nanostructured polymeric materials can be readily prepared via the polymerization of these nonionic bicontinuous microemulsions (abstract). The amphiphilic PEO macromonomers can undergo a fast micellar polymerization in water (page 6421, first column, first paragraph).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use C1-PEO-C11-MA-40, a non ionic surfactant, as taught by Liu for the surfactant used in the porous microemulsion taught by Chieng because the C1-PEO-C11-MA-40 non ionic surfactant can undergo a fast micellar polymerization in water as taught by Liu. One would have a reasonable expectation of success because the emulsions taught by Lui and Chieng both contain MMA, HEMA and EGDMA, with the only substitution being the surfactant used in Chieng for the C1-PEO-C11-MA-40 surfactant recited by Liu.

Vandamme teaches eye drops are the most used dosage form by ocular route, in spite of low bioavailability and the pulsed release of the drug. However, due to their intrinsic properties and specific structure, the micro emulsions are a promising dosage form for the natural defense of the eye. Micro emulsions are taught as being stable and

having a high capacity of dissolving the drugs. Micro emulsions have shown a delayed effect and an increase in the bioavailability of the drug (abstract). Microemulsions have been investigated as carriers used to find new drug delivery systems. Micro emulsions inherently provide the capacity to make soluble lipophilic drugs (page 16, first column, first paragraph). Bicontinuous systems have been proposed for a microemulsions used (page 16, first column, third paragraph). The choice of the oily phase (which is dispersed for ophthalmic drug delivery applications) is important for both the existence of microemulsions and the solubilization of the drug (page 17, second column, last paragraph). Figure 4 shows Chloramphenicol, an ophthalmic drug, being added to a mixture of the organic phase and surfactant (Table 2, Figure 4, page 20).

The '913 patent teaches an ophthalmic molding process wherein a polymer is used that is corsslinked to form a bicontinuous structure (abstract). The manufacturing product is lenses. An aqueous emulsion is formed which is then cross-linked (column 1, lines 1-5). An ophthalmic molding have at least partly bicontinuous microstructure may be obtained by making a bicontinuous microemulsion and then crosslinking the microemulsion obtained (column 1, lines 34-41). Methyl methacrylate is taught as a suitable hydrophilic comonomer (column 11, lines 15-30). HEMA is taught as a suitable hydrophilic comonomer (column 11, lines 56-65). The product is also taught to be suitable for drug delivery (column 14, lines 25-30).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the bicontinuous microemulsion taught by Chieng and Lui as an ophthalmic drug delivery device as Vandamme teaches the use of

bicontinuous microemulsions as ophthalmic drug delivery and the '913 patent teaches the use of cross-linked bicontinuous microemulsions for ophthalmic lenses and drug delivery. One would have a high expectation of success in using the bicontinuous microemulsion taught by the combination of Chieng and Lui for ophthalmic application as the ophthalmic microemulsion taught by the '913 patent can use MMA and HEMA as polymers which are the same polymers used by Chieng and Lui.

In regard to claim 1, the limitations of a bicontinuous microemulsion comprising water, a monomer and a surfactant copolymerized with said monomer to form a porous polymer with interconnected pores filled by water would be obvious over the single-phase region of the microemulsion was determined visually by titrating a specific amount of MMA, HEMA and EGDMA with the stock solution (page 1941, second column, second paragraph). The phase behaviors of the microemulsion was evaluated, and it was determined that a bicontinuous region was present in the microemulsion (page 1942, second column, first paragraph). For instance globular microstructure with the dimension of micrometers was seen. They stacked onto each other and the voids (pores) formed resembled the packing of a chromatographic column using fine particle materials. It is believed that these pores were interconnected and were water-filled spaces generated between the incompletely coalesced spherical aggregates taught by Chieng (page 1943, column 2, second paragraph). The limitation of a drug dispersed in at least said polymer matrix and releasable therefrom when said porous polymer is in contact with a liquid would be obvious over Vandamme teaching microemulsions for drug delivery devices (abstract). Vandamme further teaches the oily phase is used for

solubilization of the drug (page 17, second column, last paragraph) and a process of making an emulsion which consists of making a mixture of the organic phase, the drug and the surfactant (page 20, table 2, figure 4). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to add the drug to the hydrophobic polymer during the process of making the microemulsion, before polymerization as Vandamme teaches addition of the drug to the organic hydrophobic phase during the making of the micro emulsion and the '913 patent teaches methyl methacrylate is a hydrophobic polymer and the formation of a microemulsion before polymerization. It would be obvious to one of ordinary skill in the art at the time of the invention was made that addition of the hydrophobic drug to the hydrophobic polymer phase during the microemulsion formation would result in a final product which containing the drug in the polymer matrix. As the drug is containing in the polymeric phase of the microemulsion it would be inherent that upon contact with liquid the polymer would diffuse into the pores and be released.

Regarding claim 2, the limitation of the drug being ophthalmic would be obvious over the drug used in the microemulsion being released to the cornea (abstract) and Chloramphenicol being a drug used in the microemulsion (page 20, table 2) as taught by Vandamme.

Regarding claim 3, the limitation of the pores having a diameter of 10 to 100 nm would be obvious over the pore size ranges from about 1 to 10 nm as taught Lui (abstract).

Regarding claim 4, the limitation of water being present from 15-50%, monomer present from 5-40% and surfactant present from 10-50% would be obvious over the compositions used as found in table 1. MMA is present from 6-57%, HEMA is present from 20-54%, SDS is present from 1-14% and water is present from 4-40% as taught by Chieng (page 1942, table 1). The water and surfactant ranges taught by Chieng are within the ranges required by the instant claim. Each monomer by itself would be within the range required form said monomer recited in the instant claim. The combination of the MMA and HEMA monomers would total 60%, which is outside the 40% taught in the instant claims. Use of the about language however allows for additional polymer present outside the exact recited 40%, in which 60% would be included. There is also routine optimization of ranges through standard experimentation. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Regarding claims 5 and 6, the limitation of microemulsion further comprising a cross-linker, wherein the cross linker is EGDMA would be obvious over the inclusion of EGDMA in the formation of the microemulsion as taught by Chieng (page 1941, column 2, paragraphs 1 and 2).

Regarding claims 7 and 8, the limitation of the microemulsion comprising a polymerization initiator, wherein said initiator is a photo-initiator would be obvious over the photoinitiator, DBK, was used for initiating the microemulsion polymerization taught by Chieng (page 1942, first paragraph).

Regarding claim 10, the limitation of polymerizing comprises subjecting said microemulsion to ultraviolet radiation would be obvious over the reactor chamber operated at a wavelength of 235.7 nm as taught by Chieng (page 1942, first paragraph).

Regarding claims 11 and 12, the limitation of the monomer being ethylenically unsaturated, wherein the monomer is methyl methacrylate, 2-hydroxyethyl methacrylate or a combination would be obvious over the microemulsion compositions taught by Table 1, in which MMA and HEMA are both present as taught by Chieng (page 1942, table 1).

Regarding claims 13-15, the limitations of a surfactant being a non-ionic, being poly(ethylene oxide)-macromonomer, and wherein the surfactant is C1-PEO-C11-MA-40 would be obvious over the bicontinuous microemulsion using the macromonomer C1-PEO-C11-MA-40 as a polymerizable nonionic surfactant as taught by Liu (abstract).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chieng et al (publication date: 1995), Vandamme (publication date: 2002), Lui (publication date: 1997) and US 6,039,913 (patent date: 03/21/2000) as applied to claims 1-8 and 10-15 above, and further in view of Havermeyer et al. (previously cited 07/14/2009, publication date: 10/05/2000).

As mentioned in the above 103(a) rejection, all the limitations of claims 1-8 and 10-15 are taught by the combination of Chieng, Vandamme, Lui and the '913 patent. The combination of references does not teach DMPA (2,2-dimethoxy-2-phenylacetophenone) as the photoinitiator.

Havermeyer teaches poly(methyl methacrylate) (PMMA) containing residual monomer and doped with the photoinitiator 2,2-dimethoxy-2-phenylacetophenone (DMPA) is a photosensitive system for light in the ultraviolet (UV) range. In illuminated regions DMPA molecules decay into free radicals and trigger polymerization reactions of the residual monomer. The light generated free radicals induce polymerization (page 201, first column, first paragraph). This meets the limitations of claim 9.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use DMPA as the photoinitiator as taught by Havermeyer in the microemulsion taught by the combination of Chieng, Vandamme, Lui and the '913 patent because DMPA is a UV activated photoinitiator capable of polymerizing methacrylate as taught by Havermeyer and the microemulsion taught by the combination of Chieng, Simamora and Lui uses a photoinitiator that is UV activated to polymerize acrylates. One would have a reasonable expectation of success in substituting one UV activated photoinitiator for another UV activated photoinitiator.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYNDSEY BECKHARDT whose telephone number is (571)270-7676. The examiner can normally be reached on Monday thru Thursday 7:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LYNDSEY BECKHARDT/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615